

Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-35. (cancelled)

Claim 36. (original) A method for screening a plurality of compounds so as to identify compounds exhibiting antidepressant activity, comprising:

- a) determining *in vitro* efficacy and EC₅₀ values for each compound using an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 or an α_5 subunit; and
- c) identifying as having antidepressant activity a compound having an EC₅₀ value determined in a) of less than 200nM and an efficacy value determined in a) of greater than the efficacy value determined in b).

Claim 37. (original) The method of Claim 36 wherein the EC₅₀ value determined using said $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or said $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor is less than 150 nM.

Claim 38. (original) The method of Claim 37 wherein the *in vitro* efficacy measured at said $\alpha_2\beta_3\gamma_2$ or said $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 20%.

Claim 39. (original) The method of Claim 37 wherein the *in vitro* efficacy measured at said $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or said $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor is greater than 30%.

Claim 40. (original) The method of Claim 39 wherein the *in vitro* efficacy measured at said GABA_A receptor comprised of said α_1 subunit or said α_5 subunit is less than 20%.

Claim 41. (original) The method of Claim 36 wherein the *in vitro* efficacy measured at said $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or said $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor is greater than 20%.

Claim 42. (original) The method of Claim 36 wherein the *in vitro* efficacy measured at said $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or said $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor is greater than 30%.

Claim 43. (original) The method of Claim 42 wherein the *in vitro* efficacy measured at said GABA_A receptor comprised of said α_1 subunit or said α_5 subunit is less than 20%.

Claim 44. (original) The method of Claim 36 wherein the GABA_A receptor comprised of said α_1 subunit is an $\alpha_1\beta_2\gamma_2$ GABA_A subtype receptor or the GABA_A receptor comprised of said α_5 subunit is an $\alpha_5\beta_3\gamma_2$ GABA_A subtype receptor.

Claim 45. (original) A method for screening compounds for antidepressant activity, comprising:

- a) selecting compounds having a binding affinity less than 100 nM at any GABA_A receptor;
- b) determining *in vitro* efficacy and EC₅₀ values for the selected compounds using an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- c) determining *in vitro* efficacy for the selected compounds using a GABA_A receptor comprised of an α_1 or an α_5 subunit; and
- d) identifying as having antidepressant activity a compound having an EC₅₀ as determined in b) of less than 200nM and an efficacy value as determined in b) greater than the efficacy value determined in c).

Claim 46. (original) A method for screening compounds for antidepressant activity, comprising:

- a) determining *in vitro* efficacy and EC₅₀ values for each compound using an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 or an α_5 subunit;
- c) determining *in vivo* effect of said compound in an animal model indicative of antidepressant activity;
- d) determining the *in vivo* effect of said compound in an animal model indicative of sedative effects; and
- e) identifying as an antidepressant a compound that produces an EC₅₀ value as determined in a) of less than 200nM, and an efficacy value as determined in b) greater than the efficacy value from c), and (i) produces a statistically significant ($p < 0.05$) positive effect in the animal model indicative of antidepressant activity and (ii) does not produce a statistically significant effect in the animal model indicative of sedative effects.

Claim 47. (original) A method for screening compounds for antidepressant activity, comprising:

- a) selecting test compounds having a binding affinity less than 100 nM at any GABA_A receptor;
- b) determining *in vitro* efficacy and EC₅₀ value for each test compound using an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- c) determining *in vitro* efficacy value for each test compound at a GABA_A receptor comprised of an α_1 subunit or an α_5 subunit;
- d) determining the *in vivo* effect of each test compound in an animal model indicative of antidepressant activity;
- e) determining the *in vivo* effect of each test compound in an animal model indicative of sedative effects; and
- f) identifying as an antidepressant a compound that produces: an EC₅₀ value as determined in b) of less than 200nM, an efficacy value as determined in c) greater than the efficacy value from d), and (i) produces a statistically significant ($p < 0.05$) positive effect in the animal model indicative of antidepressant activity and (ii) does not produce a

statistically significant effect in the animal model indicative of sedative effects.

Claims 48-50. (cancelled)

Claim 51. (new) A method for screening a plurality of compounds so as to identify compounds exhibiting antidepressant activity, comprising:

- a) determining *in vitro* efficacy and EC₅₀ values for each compound using an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 or an α_5 subunit; and
- c) identifying as having antidepressant activity a compound that is a partial agonist and has an EC₅₀ value determined in a) of less than 200nM and an efficacy value determined in a) of greater than the efficacy value determined in b).